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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/599,460

09/28/2006

Yoko Yamagata

TSU-009

9304

38051

7590

07/09/2009

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EXAMINER

BURKHART, MICHAEL D

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

07/09/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/599,460	Applicant(s) YAMAGATA ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/26/2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 5, 6 and 14-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 7-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 September 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/26/07; 4/26/09</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of the species of CaMKII α recited in claim 4 in the reply filed on 4/26/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5, 6 and 14-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/26/2009.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (PNAS, 2003).

Wang et al teach the generation of mutant CaMKII α proteins that are considered inactive in the presence of inhibitors specific for the mutant CaMKII α mutants. The mutants were prepared by changes in the kinase domain, and the activity blocked by the inhibitors was the kinase activity. See the abstract, page 4287, second column, third full ¶, Fig. 1, page 4288, first column, third full ¶ and fifth full ¶ to the second column. The mutant CaMKII proteins could be

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inactivated in transgenic mice (Fig. 2), and Wang et al teach the creation of knock-in animals (page 4292, first column, first full ¶). The transgenic mice displayed a significant increase in Ca²⁺ activity relative to WT mice (Fig. 2, ¶ linking first and second columns, page 4289), thus it is considered that the mutant CaMKII proteins maintained the ability to bind calmodulin and to multimerize, i.e. the mutants were functional as WT proteins in the absence of the inhibitor.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Hanson et al (Neuron, 1994, of record).

Hanson et al teach the creation of a K42M or K42R catalytic domain mutants in CaMKII α (termed CaMKII^I) that inactivate the kinase activity of the protein but retain the ability to multimerize and bind calmodulin. See Figs. 1 and 2 and page 945, first column to page 946, first column. The mutants were expressed in COS cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elgersma et al (Neuron, 2002, of record), Wang et al (PNAS, 2003), Hanson et al (Neuron, 1994, of record) and Sutoo et al (Brain Res., 2002, of record).

Elgersma et al teach the generation of mutant CaMKII α knock-in mice, wherein the autophosphorylation activity of CaMKII has been altered. The method used was a well-known gene targeting protocol involving ES cell technology. See the abstract and ¶ linking the first and second columns, page 494. Elgersma et al further teach that, in general, the disruption of CaMKII activity results in spatial learning defects, and that training leads to activation of CaMKII (¶ linking first and second columns, page 498).

The teachings of Wang and Hanson et al are as above and applied as before.

None of Elgersma, Wang, or Hanson et al teach that impairment of the CaMKII α kinase activity would result in knock-in animals having lower activity in the nuclear accumbens while retaining activity in the cerebral cortex and corpus striatum.

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Sutoo et al teach that CaMKII is highly expressed in the nucleus accumbens but only moderately expressed in the globular pallidus (a component of the corpus striatum) (page 7, first column, third full ¶).

The claimed knock-in animals are essentially disclosed by Wang et al with the exception of the phenotype limitation in claim 2. The use of the CaMKII^I mutants of Hanson et al with the knock-in animals of either Wang or Elgersma et al would have been obvious to one of skill in the art because of the known benefit of generating knock-in animals expressing CaMKII α mutants as taught by both Wang and Elgersma et al. The ordinary skilled artisan would have been motivated to do so as it was an art-recognized goal to determine the physiological role of CaMKII in memory and learning by the generation of knock-in mice, wherein the phenotype of such a knock-in can be observed. Given the results of Sutoo et al, it would be expected that neuronal activity in the nucleus accumbens might be affected CaMKII mutations as CaMKII α is highly expressed in this region, whereas it is only moderately expressed in a portion of the corpus striatum. Furthermore, CaMKII α is closely associated with neuron activity and has three different domains (kinase domain, regulatory domain, and association domain) that regulate nerve function via different activities such as autophosphorylation, kinase activity, Ca²⁺/calmodulin binding, and association with other CaMKII isoforms. It would thus not be unexpected that different regions of the brain (e.g. the nucleus accumbens and cerebral cortex) might be affected differently by CaMKII α mutations, particularly given the results of Wang and Elgersma et al regarding the affects of CaMKII α inactivation/mutation on the complex processes of learning and memory.

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The totality of the prior art teaches the predictable generation of CaMKII α mutants with the claimed activity, and the predictable use of such mutants to generate knock-in mice expressing the mutants. All of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (*See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)). People of ordinary skill in the art will be highly educated individuals, possessing advanced degrees, including M.D.'s and Ph.D.'s. They will be medical doctors, scientists, or engineers. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology, cloning, and the creation of transgenic animals. Therefore, the level of ordinary skill in this art is high. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhardt/
Primary Examiner, Art Unit 1633